

BIOCHEMICAL REACTION CARTRIDGE

FIELD OF THE INVENTION AND RELATED ART

The present invention relates to a biochemical
5 reaction cartridge that can be incorporated in an
apparatus for analyzing a cell, a microorganism, a
chromosome, a nucleic acid, etc., in a specimen by
utilizing a biochemical reaction, such as
antigen-antibody reaction, or nucleic acid
10 hybridization.

Most analyzers for analyzing specimens, such as
blood, use an immunological procedure utilizing an
antigen-antibody reaction or a procedure utilizing
nucleic acid hybridization. For example, protein or
15 single-stranded nucleic acid, such as antibody or
antigen, which specifically hybridizes with a material
or substance to be detected, is used as a probe and is
fixed on a surface of a solid phase, such as fine
particles, beads or a glass plate, thus effecting the
20 antigen-antibody reaction or nucleic acid
hybridization. Then, for example, an antigen-antibody
compound or double-stranded nucleic acid is detected
by a labeled antigen or labeled nucleic acid, which
causes a specific interaction, such that a labeled
25 material having a high detection sensitivity, such as
an enzyme, a fluorescent material or a luminescent
material, is supported, thus effecting detection of

presence or absence of the material to be detected or a quantitative determination regarding the detected material.

As an extension of these technologies, e.g., U.S. Patent No. 5,445,934 discloses a so-called DNA (deoxyribonucleic acid) array, wherein a large number of DNA probes having mutually different base sequences are arranged on a substrate in an array form.

Further, Anal. Biochem., 270(1), pp. 103 - 111 (1999) discloses a process for preparing a protein array, like the DNA array, such that various species of proteins are arranged on a membrane filter. By using these DNA and protein arrays and the like, it has become possible to test a large number of items at the same time.

Further, in various methods of the specimen analysis, in order to alleviate the contamination by the specimen, promote reaction efficiency, reduce the size of the apparatus, and facilitate the operation, there have been also proposed disposable biochemical reaction cartridges in which a necessary reaction is performed. For example, Japanese Laid-Open Patent Application (JP-A) (Tokuhyo) Hei 11-509094 discloses a biochemical reaction cartridge, including DNA array, in which a plurality of chambers are disposed and a solution is moved by a differential pressure, so as to permit a reaction, such as extraction, amplification

or hybridization of DNA in a specimen, within the cartridge.

As a method of supplying a reagent with respect to the biochemical reaction cartridge, JP-A 5 2000-266759 discloses that a reagent is supplied from an external reagent bottle to a disposable analysis cassette. Further, JP-A (Tokuhyo) Hei 11-509094 discloses that a reagent is incorporated in a chamber in advance.

10 However, in the case of externally supplying the reagent, a plurality of reagents must be prepared separately from the biochemical reaction cartridge, and if the number of test items is large, the number of necessary reagents is also increased. As a result, 15 replenishment of the reagents becomes complicated and there is a possibility of erroneously selecting the species of the reagents. Further, when the reagent is incorporated into the chamber of the biochemical reaction cartridge, it is possible that a reaction 20 different from that intended can occur if the reagent flows into a passage or another chamber due to an environmental change at the time of storage or conveyance, or vibration during conveyance.

25 SUMMARY OF THE INVENTION

An object of the present invention is to provide a biochemical reaction cartridge, having solved the

above-described problems, which eliminates the inconvenience of replenishment of a reagent and erroneous selection of the species of reagent and does not cause the reagent in a chamber to flow into a
5 passage or vibration at the time of storage or conveyance.

Another object of the present invention is to provide a biochemical reaction apparatus for effecting a biochemical reaction by using the biochemical
10 reaction cartridge.

According to the present invention, there is provided a biochemical reaction cartridge, comprising:
a reaction portion, comprising a chamber and a passage, for effecting a biochemical reaction, and
15 a solution storage portion, which is isolated or separated from the reaction portion, for storing a solution at a position corresponding to the chamber,
wherein the cartridge is provided with a penetrable partition member disposed between the
20 solution storage portion and the reaction portion so as to move the solution from the solution storage portion to the chamber of the reaction portion.

These and other objects, features and advantages of the present invention will become more apparent
25 upon a consideration of the following description of the preferred embodiments of the present invention taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a perspective view of an embodiment of the biochemical reaction cartridge according to the present invention.

Figure 2 is a plan view of a solution storage portion.

Figure 3 is a partial sectional view of the biochemical reaction cartridge at the time of storage.

Figure 4 is a partial sectional view of the biochemical reaction cartridge in such a state that a valve stem (rod) is pressed by first-stage pushing.

Figure 5 is a partial sectional view of the biochemical reaction cartridge in such a state that a valve stem is pressed by second-state pushing.

Figure 6 is a plan view of a reaction portion.

Figure 7 is a block diagram of a treatment apparatus for controlling the movement of a solution and various reactions within the biochemical reaction cartridge.

Figures 8A and 8B show a flow chart of a first treatment procedure.

Figure 9 is a longitudinal sectional view of a part of the chambers shown in Figure 6.

Figure 10 is a longitudinal sectional view of another part of the chambers shown in Figure 6.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Below, the present invention is described more specifically with reference to the drawings.

Figure 1 is a perspective view of a biochemical
5 reaction cartridge in this embodiment. Referring to
Figure 1, the cartridge has a two-layer structure
including a reaction portion 1, where a reaction is
effected, and a solution storage portion 2 disposed
thereon for storing solutions, such as a reagent and a
10 cleaning agent.

A body of each of the reaction portion 1 and the
solution storage portion 2 comprises a synthetic
resin, such as polymethyl methacrylate (PMMA),
acrylonitrile-butadiene-styrene (ABS) copolymer,
15 polystyrene, polycarbonate, polyester or polyvinyl
chloride. In the case where an optical measurement is
required, the material for the body of the reaction
portion 1 is required to be a transparent or
semitransparent plastic.

20 At an upper portion of the reaction portion 1, a
specimen port 3 for injecting a specimen, such as
blood, by a syringe (injector) is disposed and sealed
up with a rubber cap. On both side surfaces of the
reaction portion 1, there is a plurality of nozzle
25 ports 4, into which nozzles are injected to apply or
reduce pressure in order to move a solution in the
reaction portion 1. A rubber cap is fixed on each of

the nozzle ports 4. The other side surface of the reaction portion 1 has a similar structure.

Further, to an upper portion of the solution storage portion 2, 3 aluminum foil sheets are applied
5 for blocking an upper portion of a solution storage chamber described later. The reaction portion 1 and the solution storage portion 2 are bonded to each other through ultrasonic fusion. Incidentally, the reaction portion 1 and the solution storage portion 2
10 are separately prepared, and the solution storage portion 2 may be superimposed on the reaction portion 1 at the time of use.

A bar code label 40 for identifying the type of cartridge is adhered to the side surface of the
15 biochemical reaction cartridge. When the biochemical reaction cartridge is set to a treatment apparatus described later, the bar code is read and the type of the cartridge is identified from the result. Setting of the treatment apparatus is automatically performed,
20 so as to effect an appropriate treatment procedure.

Figure 2 is a plan view of the solution storage portion 2 of Figure 1. Referring to Figure 2, the solution storage portion 2 is provided with independent chambers 6a to 6m, each containing a
25 solution. In the chambers 6 and 6b, a first hemolytic agent containing EDTA (ethylenediaminetetraacetic acid) for destructing cell wall and a second hemolytic

agent containing a protein-modifying agent, such as a surfactant, are stored, respectively.

In the chamber 6c, particles of magnetic material coated with silica, by which DNA is adsorbed, are
5 stored. In the chambers 6l and 6m, a first extraction cleaning liquid and a second extraction cleaning liquid, which are used for purifying DNA at the time of extraction of DNA, are stored, respectively.

An eluent, comprising a buffer of low
10 concentration salt, for eluting DNA from the magnetic particles, is stored in the chamber 6d. A mixture liquid for PCR (polymerase chain reaction) comprising a primer, polymerase, a dNTP (deoxyribonucleotide triphosphate), a buffer, Cy-3dUTP containing a
15 fluorescent agent, etc., is stored in the chamber 6g. In the chambers 6h and 6j, a cleaning agent containing a surfactant for cleaning a fluorescence-labeled specimen DNA, which is not subjected to hybridization, and a fluorescence label are stored. In the chamber
20 6i, alcohol for drying the inside of a chamber including a DNA microarray, which is described below, is stored. The respective chambers 6a to 6m are provided with sharp-pointed valve stems (rods) 7a to 7m, respectively, described below, for penetrating the
25 sheets.

Figure 3 is a sectional view showing a storage state in the biochemical reaction cartridge.

Referring to Figure 3, the valve stem 7 provided with a cut 8 is injected into the chamber 6 of the solution storage portion 2, which contains a solution, and is supported by two o-rings. The bottom of the solution chamber 6 is blocked by an aluminum foil sheet 10. A sealing member 12 is disposed between the chamber 6 and the chamber 11 of the reaction portion 1, so as to make it impossible for air to enter and exit. Changes in volume of the solution and air and in pressure due to the environment can be accommodated by the deformation of the aluminum foil sheet 10, so that the solution in the chamber 6 cannot unexpectedly enter the reaction portion 1.

Figure 4 illustrates a state in which, after a tester injects a liquid specimen, such as blood, from the specimen port 3 and sets the biochemical reaction cartridge to a treatment apparatus described below, a robot arm (not shown) presses the valve stem 7 by first-stage pushing with a shorter pressing rod 13a of a rod needle 13 to tear the aluminum foil sheet, thus starting the movement of the solution from the chamber 6 to the chamber 11. In this state, the two O-rings 8 are located in the cut 8 of the valve stem 7, so that the chamber 6 communicates with outside air. Accordingly, the solution can be moved smoothly.

As described above, the biochemical reaction cartridge has the penetrable aluminum sheet 10 as a

partition member, so that only by pressing the pressing rod 13a of the tool needle 13 toward the reaction portion 1 it is possible to readily cause the solution to flow from the chamber 6 into the chamber 11 without the tool needle 13 coming into contact with the solution. Incidentally, in this embodiment, immediately under the position of the chamber of the solution storage portion 2, a corresponding chamber of the reaction portion 1 is located, but there is no harm in shifting the corresponding chamber from the position immediately under the chamber of the solution storage portion 2 if, e.g., a passage is provided therebetween.

In this embodiment, the chamber of the reaction portion 1 and the chamber of the solution storage portion 2 are in a one-to-one relationship, but a plurality of solution storage chambers may be provided per one chamber for the reaction portion 1. Further, in this embodiment, the solution is moved from the solution storage chamber to a blank chamber of the reaction portion 1, but it may be moved from the solution storage chamber to a chamber of the reaction portion 1 already containing a specimen or a solution during treatment. Further, in this embodiment, the aluminum foil sheet 10 is used as the partition member, but the partition member per se may be a non-penetrable member if it is provided with an

ordinary valve, and the valve is placed in a penetrable state, i.e., an open state so as to permit the flow of the solution into the chamber of the reaction portion 1.

5 Next, the tester extracts the tool needle 13 from the treatment apparatus once by using the robot arm and turns the tool needle 13 upside down, followed by further pressing the valve stem 7 by second-stage pushing with a longer pressing rod 13b, as shown in
10 Figure 5. As a result, air is sealed up by the upper O-ring 9 to permit the movement of the solution in the reaction portion 9 to permit the movement of the solution in the reaction portion 1, as described below. The tester performs this step with respect to
15 all the chambers 6a to 6m. As described above, the solution can be caused to flow into the chamber by the first-stage pushing, and the chamber can be sealed up by the second-stage pushing, so that it is possible to effect the flow of the solution into the chamber 11
20 and seal off the chamber 11 at the same time only by simple pushing operations. Further, the above-described tool needle may be provided in the biochemical reaction cartridge.

Figure 6 is a plan view of the reaction portion
25 1. Referring to Figure 6, 10 nozzle ports 4a to 4j are provided on one side surface of the reaction portion 1. On the other side surface, 10 nozzle ports

4k to 4t are provided. The respective nozzle ports 4a to 4t communicate with chambers 11a to 11t, which are portions or sites for storing the solution or causing a reaction, through corresponding air passages 14a to 14t for air flow, respectively.

In this embodiment, however, the nozzle ports 4n, 4p, 4q and 4s are not used. These nozzle ports do not communicate with the chambers and are used as reserve ports. More specifically, in this embodiment, the nozzle ports 4a to 4j communicate with the chambers 11a to 11j through the passages 14a to 14j, respectively. On the other side surface, the nozzle ports 4k, 4l, 4m, 4o, 4r and 4t communicate with the chambers 11k, 11l, 11m, 11o, 11r and 11t through the passages 14k, 14l, 14m, 14o, 14r and 14t, respectively.

The specimen port 3 communicates with a chamber 16. The chambers 11a, 11b, 11c and 11k communicate with the chamber 16, the chambers 11g and 11o communicate with a chamber 17, and the chambers 11h, 11i, 11j, 11r and 11t communicate with a chamber 18. Further, the chamber 16 communicates with the chamber 17 via a passage 19, and the chamber 17 communicates with the chamber 18 via a passage 20. With the passage 19, the chambers 11d, 11e, 11f, 11l and 11m communicate via passages 15d, 15e, 15f, 15l and 15m, respectively. At a bottom (undersurface) of the

chamber 18, a square hole is provided. A DNA
microarray 21, on which several tens to several
hundreds of thousand of different species of DNA
probes are arranged at high density on a surface of a
5 solid phase, such as a glass plate having a size of
ca. one square centimeter, with the probe surfaces up,
is attached to the square hole.

It is possible to test a large number of genes at
the same time by hybridizing with the specimen DNA
10 using the microarray 21.

The DNA probes are regularly arranged in a
matrix form, and an address (position determined by
the row and column numbers on the matrix) of each of
the DNA probes is readily read as information. The
15 genes to be tested include, e.g., genetic polymorphism
of each individual in addition to infections viruses,
bacteria and disease-associated genes.

In the chambers 11a and 11b of the reaction
portion 1, a first hemolytic agent and a second
20 hemolytic agent to be moved from the chambers 6a and
6b and the solution storage portion 2 are stored,
respectively. In the chamber 11c, magnetic material
particles to be moved from the chamber 6 are stored.
In the chambers 11l and 11m, a first extraction
25 cleaning liquid and a second extraction cleaning
liquid to be moved from the chambers 6l and 6m are
stored, respectively. An eluent flowing from the

chamber 6d is stored in the chamber 11d, a mixture liquid necessary for PCR (polymerase chain reaction) moved from the chamber 6g is stored in the chamber 11g. In the chambers 11h and 11j, cleaning agents to
5 be moved from the chambers 6h and 6j are stored, respectively. In the chamber 11i, alcohol to be moved from the chamber 6i is stored.

The chamber 11e is a chamber in which dust, other than DNA from blood, accumulates, the chamber 11f is a
10 chamber in which waste of the first and second extraction cleaning liquids in the chambers 11l and 11m accumulates, the chamber 11r is a chamber in which waste of the first and second cleaning agents accumulates, and the chambers 11k, 11o and 11t are
15 blank chambers provided for preventing the solution from flowing into the nozzle ports.

Figure 7 is a schematic view of the treatment apparatus for controlling the movement of the solution within the biochemical reaction cartridge and various
20 reactions.

The biochemical reaction cartridge is mounted on a table 22. Further, an electromagnet 23 to be actuated at the time of extracting DNA or the like from the specimen in the cartridge 1, a Peltier
25 element 24 for effecting temperature control at the time of amplifying DNA from the specimen through a method such as PCR (polymerase chain reaction), and a

Peltier element 25 for effecting temperature control at the time of performing a hybridization between the amplified specimen DNA and the DNA probe on the DNA microarray within the cartridge 1 and at the time of
5 cleaning or washing the specimen DNA, which is not hybridized, are disposed on the table 22 and connected to a control unit 26 for controlling the entire treatment apparatus. Further, the robot arm (not shown) for pushing down the valve stem by moving the
10 tool needle 13 above a predetermined chamber on the cartridge, as described above, and a bar code reader (not shown) for reading the bar code label applied to the cartridge are provided in the treatment apparatus.

At both side surfaces of the table 22, an
15 electric (motor-driven) syringe pumps 27 and 28 and pump blocks 31 and 32, each of which is a port for discharging or sucking in air by these pumps 27 and 28 and is provided with 10 pump nozzles 29 or 30 on its side surface, are disposed. Between the electric
20 syringe pumps 27 and 28 and the pump nozzles 29 and 30, a plurality of known electric switching (selector) valves (not shown) are disposed and connected to the control unit 26 together with the pumps 27 and 28. The control unit 26 is connected to an input unit 33
25 to which inputting by a tester is performed. The control unit 26 controls the pump nozzles 29 and 30, so that each of the respective 10 pump nozzles is

selectively opened and closed with respect to the electric syringe pumps 27 and 28, respectively.

When the solution is moved from the solution storage portion 2 to the reaction portion 1 and a
5 treatment start signal is inputted, extraction and amplification of DNA or the like are performed within the reaction portion 1. Further, hybridization between the amplified specimen DNA and DNA probes on the DNA microarray disposed in the reaction portion 1
10 and cleaning of the fluorescence-labeled specimen DNA, which is not hybridized, and the fluorescence label are performed.

In this embodiment, when the tester injects blood as a specimen into the reaction portion through the
15 rubber cap of the specimen port 3 by a syringe or an injector, the blood flows into the chamber 16. Thereafter, the tester places the biochemical reaction cartridge on the table 22 and moves the pump blocks 31 and 32 in directions indicated by the arrows in Figure
20 7 with a mechanism (not shown) by operating a lever (not shown), whereby the pump nozzles 29 and 30 are injected into the corresponding nozzle ports 4 of the reaction portion 1.

As described with reference to Figure 6, the
25 nozzle ports 4 are concentrated at two surfaces, i.e., both side surfaces, of the biochemical reaction cartridge, so that it is possible to simplify shapes

and arrangements of the electric syringe pumps 27 and 28, the electric switching valves, the pump blocks 31 and 32 containing the pump nozzles 29 and 30, etc.

Further, by effecting such a simple operation that the
5 cartridge is sandwiched between the pump blocks 31 and 32 at the same time while ensuring necessary chambers and passages, it is possible to inject the pump nozzles 29 and 30 and simplify the structure of the pump blocks 31 and 32. Further, all the nozzle ports
10 4a to 4t are disposed at an identical level, i.e., are arranged linearly, whereby all the heights of the passages 14a to 14t connected to the nozzle ports 4a to 4t become equal to each other. As a result, preparation of the passages 14a to 14t becomes easy.

15 Further, in the treatment apparatus shown in Figure 7, in the case where the length of the pump blocks 31 and 32 is increased n times the original length with respect to n biochemical reaction cartridges, when n cartridges are arranged in series,
20 it is possible to perform a necessary step with respect to all the n cartridges at the same time. As a result, a biochemical reaction can be performed in a large number of biochemical reaction cartridges with a very simple apparatus structure.

25 When the tester performs the steps of flowing of the solution into the chamber and hermetically sealing the chamber described with reference to

Figures 4 and 5 and then inputs a treatment start instruction at the input unit 33, the bar code label applied to the biochemical reaction cartridge is first read by the bar code reader (not shown) of the treatment apparatus. In the treatment apparatus, treatment sequences necessary for the respective types of cartridges are memorized in advance. When the type of cartridge is identified by the read bar code, the contents and procedures of treatment necessary for the cartridge are automatically determined to start the treatment. When the bar code cannot be read or the read bar code is not a predetermined bar code, the tester can also manually input treatment steps by the input unit 33.

Figures 8A and 8B show a flow chart for explaining an example of a treatment procedure in the treatment apparatus in this embodiment.

Referring to Figure 8A, in step S1, the first hemolytic agent is moved from the solution storage chamber 6a to the chamber 11a of the reaction portion 1 by injecting the solution and hermetic sealing, as described with reference to Figures 4 and 5. In step S2, the control unit 26 opens only the nozzle ports 4a and 4b, and air is discharged from the electric syringe pump 27 and sucked in the reaction portion 1 from the electric syringe pump 28, whereby the first hemolytic agent is injected from the chamber 11a into

the chamber 16 containing blood. At this time, by
controlling air suction from the pump 28 so as to
start 10 - 200 msec after initiation of the air
discharge from the pump 27, the solution can flow
5 smoothly without splashing or scattering at its
leading end, although this depends on the viscosity of
the hemolytic agent and a resistance of the passage.

As described above, by shifting the timing of the
supply and suction of air so as to control a manner in
10 which the pressure is applied and reduced, it is
possible to cause the solution to flow smoothly. In a
preferred embodiment, the solution can be caused to
flow even more smoothly by controlling air suction
from the electric syringe pump 28 such that it is
15 linearly increased from the initiation of the air
discharge from the pump 27. Further, it becomes
possible to alleviate the pressure generated in the
reaction portion 1 by applying and reducing pressure
in combination. As a result, it is also possible to
20 intentionally prevent the solution from flowing into a
branched passage or chamber during the movement
thereof. This is also true in the case of a
subsequent liquid movement.

The air supply control can be readily realized by
25 using the electric syringe pumps 27 and 28. More
specifically, after only the nozzle ports 4a and 4o
are opened, discharge and suction of air are repeated

alternately by the syringe pumps 27 and 28 to cause a repetitive flow and return of the solution of the chamber 6 in the passage 19, thus stirring the solution. Alternatively, the solution can be stirred
5 while continuously discharging air from the pump 28 to generate bubbles.

Figure 9 is a sectional view of the reaction portion 1 shown in Figure 6 along a cross-section intersecting the chambers 11a, 16 and 11k, and shows
10 such a state that the nozzle port 4a is pressurized by injecting therein the pump nozzle 29 and the nozzle port 4k is reduced in pressure by injecting therein the pump nozzle 30, whereby the first hemolytic agent in the chamber 11a flows into the chamber 16
15 containing blood.

Referring again to Figure 8A, in step S4, only the nozzle ports 4b and 4k are opened and the second hemolytic agent in the chamber 11b is caused to flow into the chamber 16 in the same manner as in the case
20 of the first hemolytic agent. Similarly, in step S5, the magnetic particles in the chamber 11, after being moved from the chamber 6c to the chamber 11, are caused to flow into the chamber 16. In steps S4 and S6, stirring is performed in the same manner as in
25 step S2. In step S6, DNA resulting from dissolution of cells in steps S2 and S4 attaches to the magnetic particles.

Thereafter, in step S7, an electromagnet 23 is turned on and only the nozzle ports 4e and 4k are opened. Then, air is discharged from the electric syringe pump 28 and sucked in from the pump 27 to move
5 the solution from the chamber 16 to the chamber 11e. At the time of movement, the magnetic particles and DNA are trapped in the passage 19 on the electromagnet 23. The suction and discharge by the pumps 27 and 28 are alternately repeated to reciprocate the solution
10 two times between the chambers 16 and 11e, whereby a trapping efficiency of DNA is improved. The trapping efficiency can be further improved by increasing the number of reciprocations. In this case, however, the time of treatment is increased by the amount of time
15 it takes to perform the additional reciprocations.

As described above, DNA is trapped in a flowing state on such a small passage having a width of about 1 - 2 mm and a height of about 0.2 - 1 mm by utilizing the magnetic particles, so that DNA can be trapped
20 with a high efficiency. This is also true for RNA and proteins.

Then, in step S8, the electromagnet 23 is turned off and only the nozzle ports 4f and 4l are opened. Thereafter, air is discharged from the electric
25 syringe pump 28 and sucked in from the pump 27 to move the first extraction cleaning liquid from the chamber 11l to the chamber 11f. At this time, the magnetic

particles and DNA trapped in step S7 are moved together with the extraction cleaning liquid, whereby cleaning is performed. After the reciprocation is performed two times in the same manner as in step S7,
5 the electromagnet 23 is turned on, and the reciprocation is similarly performed two times to recover the magnetic particles and DNA in the passage 19 on the electromagnet 23 and return the solution to the chamber 11l.

10 In step S11, cleaning is further performed in the same manner as in step S5 by using the second extraction cleaning liquid in the chamber 11m, after being moved from the chamber 6m to the chamber 11m in step S10, in combination with the nozzle ports 4f and
15 4m.

In step 12, the eluent is moved from the chamber 6d to the chamber 11d. In step S13, only the nozzle ports 4d and 4o are opened while the electromagnet 23 is kept on and air is discharged from the pump 27 and
20 sucked in from the pump 28, whereby the eluent in the chamber 11d is moved to the chamber 17.

At this time, the magnetic particles and DNA are separated by the action of the eluent, so that only the DNA is moved together with the eluent to the
25 chamber 17, and the magnetic particles remain in the passage 19. Thus, extraction and purification of the DNA are performed. As described above, the chambers

11l and 11m containing the extraction cleaning liquids and the chamber 11f containing a waste liquid after the cleaning are separately provided, so that it becomes possible to effect extraction and purification
5 of the DNA in the biochemical reaction cartridge.

Next, in step S14, the PCR agent is moved from the chamber 6g to the chamber 11g. In step S15, only the nozzle ports 4g and 4o are opened, and air is discharged from the electric syringe pump 27 and
10 sucked in from the pump 28 to cause the PCR agent in the chamber 11g to flow into the chamber 17. Further, only the nozzle ports 4g and 4t are opened and air discharge and suction by the pumps 27 and 28 are repeated alternately to cause the solution in the
15 chamber 16 to flow into the passage 20. Thereafter, the returning operation is repeated to effect stirring. Then, the Peltier element 24 is controlled to retain the solution in the chamber 17 at 96 °C for 10 min. Thereafter, a cycle of heating at 96 °C/10
20 sec, 55 °C/10 sec, and 72 °C/1 min. is repeated 30 times, thus subjecting the eluted DNA to PCR to amplify the DNA.

In step S16, only the nozzle ports 4g and 4t are opened and air is discharged from the electric syringe
25 pump 27 and sucked in from the pump 28 to move the solution in the chamber 17 to the chamber 18. Further, by controlling the Peltier element 25, the

solution in the chamber 18 is kept at 45 °C for 2 hours to effect the hybridization. At this time, discharge and suction of air by the pumps 27 and 28 are repeated alternately to move the solution in the
5 chamber 18 to the passage 15t. Thereafter, the hybridization proceeds while effecting stirring by repeating the returning operation.

Then, after the first cleaning liquid is moved from the chamber 6h to the chamber 11h in a step S17,
10 in a step S18, while keeping the temperature at 45 °C, only the nozzle ports 4h and 4r are opened and air is discharged from the electric syringe pump 27 and sucked in from the pump 28 to cause the first cleaning liquid in the chamber 11h to flow into the chamber 11r
15 through the chamber 18 while moving the solution in the chamber 18 to the chamber 11r. The suction and discharge by the pumps 27 and 28 are repeated alternately to reciprocate the solution two times between the chambers 11h, 18 and 11r and finally
20 return the solution to the chamber 11h. Thus, the fluorescence-labeled specimen DNA and the fluorescence label, which are not hybridized, are cleaned.

Figure 10 is a sectional view of the reaction portion 1 shown in Figure 6 along a cross-section
25 intersecting the chambers 11h, 18 and 11r. The reaction portion 1 is pressurized by injecting the pump nozzle 29 into the nozzle port 4h and the

pressure is reduced by injecting the pump nozzle 30 into the nozzle port 4r. Figure 10 illustrates such a state that the first cleaning liquid is caused to flow into the chamber 11r through the chamber 18. The
5 chamber 11h actually communicates with the solution storage portion 2, but in Figure 10, it is illustrated as not communicating with the solution storage portion 2 by providing a ceiling thereof, for the convenience of explaining the structure.

10 Referring to Figure 8B, after the second cleaning liquid is moved from the chamber 6j to the chamber 11j in step S19, in step S20, while keeping the temperature at 45 °C, the cleaning is further effected in the same manner as in step S10 by using the second
15 cleaning liquid in the chamber 11j in combination with the nozzle ports 4j and 4r and the solution is finally returned to the chamber 11j. As described above, the chambers 11h and 11j containing the cleaning liquids and the chamber 11r containing the waste liquid after
20 the cleaning are separately provided, so that it becomes possible to extract and purify the biological material on the DNA microarray 21 in the biochemical reaction cartridge.

After alcohol is moved from the chamber 6i to the
25 chamber 11i in step S21, in step 22, only the nozzle ports 4i and 4r are opened and air is discharged from the electric syringe pump 27 and sucked in from the

pump 28 to move alcohol in the chamber 11i to the chamber 11r through the chamber 18. Thereafter, only the nozzle port 4i and 4t are opened and air is discharged from the pump 27 and sucked in from the
5 pump 28 to dry the inside of chamber 18.

Thereafter, when the tester operates a lever (not shown), the pump blocks 31 and 32 are moved away from the biochemical reaction cartridge. As a result, the pump nozzles 29 and 30 are removed from the nozzle
10 ports 4 of the cartridge. Then, the tester mounts the cartridge in a DNA microarray reader, such a known scanner, to perform the measurement and analysis.

In the above-described embodiment, the identification of the cartridge is performed by using
15 the bar code label, but may also be performed by using a two-dimensional bar code, an IC chip, PFID (radio frequency identification), etc. Further, on the basis of external dimensions of the cartridge, such as height and length, the number of recesses or
20 projections provided on the side surfaces, the upper surface and the lower surface of the cartridge, and a combination thereof, the type of the cartridge can be identified in various ways. As a result, it is possible to attain a similar effect.

25 In the above embodiment, the identification of the cartridge is performed and based on the identified type of the cartridge, and the treatment steps are

set. However, it is also possible to set a treatment sequence on the basis of the information, contents and procedures of the treatment steps, which are written in the two-dimensional bar code or the like. Further, 5 in the case of changing testing conditions, such as a reaction time, cartridge by cartridge, different treatment steps are written in a two-dimensional bar code and the bar code is adhered to the cartridge, whereby it becomes possible to effect a desired 10 reaction step with reliability.

As described above, the biochemical reaction cartridge according to the present invention has a reaction portion including a chamber and a passage and a solution storage portion, which is isolated or 15 separated from the reaction portion, for storing a solution, such as a reagent or a cleaning agent, and is constituted by such a member that it is separated for moving the solution from the solution storage portion to the reaction portion and is penetrable, or 20 that it is a penetrable member disposed at a boundary wall portion between the solution storage portion and the reaction portion, which contact each other. As a result, respective solutions can be prepared with the biochemical reaction cartridge immediately before the 25 respective treatment steps, so that the biochemical reaction cartridge has the advantage of causing an intended reaction properly without causing a reagent

in a chamber to flow into a passage or another chamber even when an environmental change or vibration occurs during a treatment step using another solution.

Further, particularly, a step of moving each of
5 the solutions in the solution storage portion to the reaction portion immediately before using the solutions is employed, so that it is possible to reliably effect the reaction without causing the solutions to flow into adjacent chambers and passages
10 even when the treatment apparatus vibrates or there is an error in pressure control during treatment in each of the steps.

Further, the treatment apparatus automatically reads the bar code label applied to the biochemical
15 reaction cartridge and identifies the type of the cartridge, thus automatically setting necessary treatment steps. Accordingly, it becomes possible to simply effect the treatment with reliability since it is not necessary for the operation to set a
20 complicated treatment procedure on all such occasions that there is a plurality of cartridge types.

Further, since the biochemical reaction cartridge of the present invention has the above-described structure, it is possible to prepare a solution
25 therein as desired. As a result, the biochemical reaction cartridge eliminates the inconvenience of replenishing a reagent and reduces an error in

selection of the type of reagent. In addition, even when an environmental change or vibration occurs at the time of storage and conveyance, the reagent in the chamber does not flow into a passage or another
5 chamber. Accordingly, the biochemical reaction cartridge can appropriately cause the intended reaction.

While the invention has been described with reference to the structures disclosed herein, it is
10 not limited to the details set forth and this application is intended to cover such modifications or changes as may come within the purposes of the improvements or the scope of the following claims.